Urinary Calculi

Vitamin C Supplementation and Urinary Oxalate Excretion

Reviewed by Dean G. Assimos, MD
Department of Urology, Wake Forest University School of Medicine, Winston-Salem, NC

[*Rev Urol.* 2004;6(3):167]

Urinary oxalate excretion plays a critical role in calcium oxalate stone formation. The majority of urinary oxalate is derived from endogenous synthesis and dietary sources. There has been an ongoing debate regarding the impact of vitamin C supplementation on urinary oxalate excretion. The 2 articles discussed here provide further information on this subject.

Effect of Vitamin C Supplements on Urinary Oxalate and pH in Calcium Stone-Forming Patients

Baxmann AC, De O G Mendonca C, Heilberg IP.

Kidney Int. 2003;63:1066-1071.

Adult calcium oxalate stone–formers were administered either 1 gram (group 1) or 2 grams (group 2) of vitamin C daily for 3 days while healthy, non–stone-forming adults (group 3) were given the 1-gram dose daily during the same time. The participants were not placed on a metabolic diet, but were instructed to refrain from consuming foods rich in vitamin C and oxalate, as well as dairy products. Twenty-four-hour urine collections were obtained at baseline and after vitamin C administration.

Urinary pH did not change after vitamin C supplementation in any of the groups. However, there were statistically significant increases in oxalate excretion in all 3 groups: 61% in group 1, 41% in group 2, and 56% in group 3. A significant increase in calcium oxalate urinary supersaturation (by Tiselius index) occurred in all groups after supplemental vitamin C intake.

Effect of Ascorbic Acid Consumption on Urinary Stone Risk Factors

Traxer O, Huet B, Poindexter J, et al.

J Urol. 2003;170:397-401.

In this double-blind, randomized, crossover study, adult calcium oxalate stone–formers and non–stone-forming adults were placed on a controlled metabolic diet for 2 6-day phases. During one of the phases, they were given 1 gram of vitamin C twice a day, and they received a placebo during the other phase. Twenty-four-hour urine specimens were collected on days 5 and 6 of each phase.

Vitamin C supplementation should not be used in managing patients with struvite calculi, because it does not reduce urinary pH, or in calcium oxalate stone–formers, as it might promote stone activity.

There were no changes in urinary pH after vitamin C ingestion in either group, although there was a moderate and statistically significant increase in urinary oxalate excretion in controls (20%) and stone-formers (33%).

Conclusions

Both of these articles clearly demonstrate that 1 to 2 grams of ascorbic acid administered daily to both normal subjects and calcium oxalate stone–formers result in no urinary pH changes but in increased oxalate excretion. Therefore, this practice should not be used in managing patients with struvite calculi, because it does not reduce urinary pH, or in calcium oxalate stone–formers, as it might promote stone activity. ■

Prostate Cancer

Prostate Cancer and Chemotherapy

Reviewed by Masood A. Khan, MD, Alan W. Partin, MD, PhD
Department of Urology, Johns Hopkins School of Medicine, Baltimore, MD

[*Rev Urol.* 2004;6(3):167-169]

Despite the increase in the number of patients presenting today with clinically localized prostate cancer who undergo definitive local therapy (either radiation therapy or radical prostatectomy), approximately 50% will experience advanced disease recurrence.[1,2] In these patients or patients presenting initially with advanced disease, suppression of androgenic activity with either surgi-

cal or medical castration (with luteinizing hormone-releasing hormone [LHRH] analogues) with or without antiandrogens is usually regarded as first-line treatment.[3,4] Unfortunately, hormonal therapy is only palliative and successful in 70% to 80% of patients, with a median duration of response of 12 to 24 months.[3,4] For patients who progress on LHRH analogues and antiandrogens, the withdrawal of antiandrogens results in a prostate-specific antigen (PSA) decline in 25% to 50% of patients.[5] Other secondary hormonal options include the use of ketoconazole and hydrocortisone, the addition of an antiandrogen in patients progressing despite administration of an LHRH analogue alone, and corticosteroids.[6] Although secondary hormonal manipulations can produce a subjective response in approximately 25% of patients, the response is only short lived (approximately 4 months).[7] This problem has prompted numerous studies to evaluate the potential use of chemotherapy for patients with hormone-resistant prostate cancer (HRPC). To this end, docetaxal, a member of the taxane family, has recently been shown to have marked activity against prostate cancer cells both in vitro and in vivo.[8,9] The following recently published articles report on the potential use of docetaxel either as monotherapy or as a part of combination therapy in the management of HRPC.

Weekly Administration of Docetaxel for Symptomatic Metastatic Hormone-Refractory Prostate Carcinoma

Gravis G, Bladou F, Salem N, et al.

Cancer. 2003;98:1627-1634.

A phase II study was conducted to investigate the clinical benefit, impact on quality of life (QOL), and tolerability of weekly docetaxel (35 mg/m^2) in 30 men (median age, 67 years) with symptomatic HRPC. Weekly docetaxel was administered intravenously for 6 weeks, followed by 2 weeks of rest. This constituted 1 cycle, and a total of 13 patients received the maximum of 4 cycles. A total of 28 patients were clinically evaluable, of which 13 patients (46%) demonstrated a clinical benefit by experiencing a reduction in pain for a median duration of 14 weeks. Furthermore, compared with baseline, QOL scores improved in all patients by the end of the first cycle. However, fatigue, dyspnea, and physical functioning results deteriorated relative to baseline at the last QOL evaluation, which was performed 15 to 30 days after completion of treatment. Of the 27 patients evaluable for a serum PSA response, 13 patients (48%) had a 50% or greater decrease in serum PSA, and 5 patients (19%) had a 75% or greater decrease that was maintained for at least 2 successive measurements taken at least 2 weeks apart. Docetaxel was generally well tolerated, with adverse effects that were mostly mild and that did not result in any patient withdrawal or deaths.

This study has shown that weekly docetaxel is an effective regimen in terms of clinical benefit, quality of life, and serum PSA response in older men with hormone-refractory prostate cancer.

Despite the absence of any demonstrable survival benefit and the small sample size, this study is encouraging because it has shown that weekly docetaxel is an effective regimen in terms of clinical benefit, QOL, and serum PSA response in older men with HRPC.

A Phase II Study of Estramustine, Docetaxel, and Carboplatin with Granulocyte-Colony-Stimulating Factor Support in Patients with Hormone-Refractory Prostate Carcinoma: Cancer and Leukemia Group B 99813

Oh WK, Halabi S, Kelly WK, et al.

Cancer. 2003;98:2592-2598.

Oh and colleagues determined the safety and efficacy of estramustine (240 mg t.i.d. on days 1–5), docetaxel (70 mg/m^2; given on day 2), and carboplatin (given on day 2; dose determined by the Calvert formula to achieve a target area under the curve of 5 mg/mL × min)[10] with granulocyte-colony-stimulating factor (G-CSF; 300–450 μg, depending on body weight, given on day 6) support in patients with HRPC. G-CSF was used to minimize the neutropenia associated with this regimen. This multicenter, cooperative group study accrued 40 patients (median age, 68 years; range, 58–75 years) who received a median of 7 cycles (each cycle repeated every 3 weeks). Of the 34 patients evaluable, 23 (68%) demonstrated a 50% or greater decline and 20 (59%) had a 75% or greater decline in serum PSA, which was confirmed by 2 consecutive measurements taken at least 4 weeks apart. The median duration of serum PSA response was 10 months. In addition, of the 21 patients with measurable disease, 1 (5%) achieved a complete response, and 10 (47%) achieved a partial response to therapy. The median duration of measurable response was 6 months, the overall median time to disease progression was 8.1 months, and the overall survival period was 19 months. This regimen was generally well tolerated, and the most common adverse effects were neutropenia in 23%, thrombocytopenia in 13%, and fatigue in 13%. This study is encouraging

for the use of docetaxel-containing combination chemotherapy, with G-CSF support, in patients with HRPC. However, because no survival benefit was demonstrated, data on the impact on QOL is needed before such a therapy is likely to receive wide acceptance. ■

References

1. Hanks GE, Krall JM, Hanlon AL, et al. Patterns of care and RTOG studies in prostate cancer: long-term survival, hazard rate observations, and possibilities of cure. *Int J Radiat Oncol Biol Phys*. 1994;28:39-45.
2. Zincke H, Oesterling JE, Blute ML, et al. Long-term (15 years) results after radical prostatectomy for clinically localized (stage T2c or lower) prostate cancer. *J Urol*. 1994;152:1850-1857.
3. Robson M, Dawson N. How is androgen-dependent metastatic prostate cancer best treated? *Hematol Oncol Clin North Am*. 1996;10:727-747.
4. Gotkas S, Crawford ED. Optimal hormonal therapy for advanced prostatic carcinoma. *Semin Oncol*. 1999;26:162-173.
5. Geller J, Albert J, Vik A. Advantages of total androgen blockade in the treatment of advanced prostate cancer. *Semin Oncol*. 1988;15:53-61.
6. Small EJ, Vogelzang NJ. Second-line hormonal therapy for advanced prostate cancer: a shifting paradigm. *J Clin Oncol*. 1997;15:382-388.
7. DiPaola RS, Patel J, Rafi MM. Targeting apoptosis in prostate cancer. *Hematol Oncol Clin North Am*. 2001;15:509-524.
8. Nehme A, Varadarajan P, Sellakumar G, et al. Modulation of docetaxel-induced apoptosis and cell cycle arrest by all-trans retinoic acid in prostate cancer cells. *Br J Cancer*. 2001;84:1571-1576.
9. Khan MA, Carducci MA, Partin AW. The evolving role of docetaxel (taxotere) in the management of androgen-independent prostate cancer. *J Urol*. 2003; 170:1709-1716.
10. Calvert H, Judson I, van der Vijgh WJ. Platinum complexes in cancer medicine: pharmacokinetic and pharmacodynamics in relation to toxicity and therapeutic activity. *Cancer Surv*. 1993;16:189-217.